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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/009,607	11/21/2001	Masahiro Imoto	1830/50520	4194

23911 7590 09/23/2005

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EXAMINER	
RAO, DEEPAK R	
ART UNIT	**PAPER NUMBER**
1624	

DATE MAILED: 09/23/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/009,607	IMOTO ET AL.	
	Examiner	Art Unit	
	Deepak Rao	1624	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *11 July 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *3-36* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) *3,4,22-25 and 34-36* is/are allowed.

6)☒ Claim(s) *5-21 and 26-33* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

This office action is in response to the amendment filed on July 11, 2005.

Claims 3-36 are pending in this application.

Withdrawn Rejections/Objections:

Applicant is notified that any outstanding rejection/objection that is not expressly maintained in this office action has been withdrawn or rendered moot in view of applicant's amendments and/or remarks.

The following rejections are under new grounds:

Upon reconsideration, it was deemed that the following rejection which was previously withdrawn, should be reinstated for the reasons provided below.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 5-21 and 26-33 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the treatment of anxiety, does not reasonably provide enablement for treating of all types of cerebral circulation diseases, neurodegenerative diseases, etc. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

In evaluating the enablement question, several factors are to be considered. Note *In re Wands*, 8 USPQ2d 1400 and *Ex parte Forman*, 230 USPQ 546. The factors include: 1) The nature of the invention, 2) the state of the prior art, 3) the predictability or lack thereof in the art, 4) the amount of direction or guidance present, 5) the presence or absence of working examples, 6) the breadth of the claims, and 7) the quantity of experimentation needed.

The scope of the method claims is not adequately enabled solely based on the activity related to $\alpha 4\beta 2$ nicotinic acetylcholine receptor activity provided in the specification. The claim language includes diseases that are known and those that are yet to be discovered, for which there is no enablement. First, the instant claims cover 'diseases' that are known to exist and those that may be discovered in the future, for which there is no enablement provided. The use disclosed in the specification is as pharmaceutical therapeutic agents having affinity for $\alpha 4\beta 2$ nicotinic acetylcholine receptors, useful to treat a laundry list of diseases, which include neurodegenerative diseases, inflammatory intestinal diseases, etc. Test assays and procedures are provided in the specification at pages 32-35, wherein the *Ki* data for some of the compounds of the invention is provided in Table 8, however, there is nothing in the disclosure regarding how this data correlates to the treatment of the diverse disorders of the instant claims. The disorders encompassed by the instant claims include neurodegenerative diseases, etc., some of which have been proven to be extremely difficult to treat. A state of the art reference, Levin et al. (AD in IDS) expresses that there are many unanswered questions regarding 'the relationship of nicotinic involvement in cognitive function to nicotinic involvement in other types of function', see page 226, col. 2. Also, Holladay et al. (AU in IDS) remarks that "The possible contributions of presently unknown subunits and the existence of more than one nAChR subtype in the same

tissue continues to present challenges..." thereby providing the complexities involved in pharmacological responses of nAChRs. Further, there is no reasonable basis for assuming that the myriad of compounds embraced by the claims will all share the same physiological properties since they are so structurally dissimilar as to be chemically non-equivalent and there is no basis in the prior art for assuming the same. Note *In re Surrey*, 151 USPQ 724 regarding sufficiency of disclosure for a Markush group.

Further, the term "neurodegenerative diseases" covers diverse disorders such as Alzheimer's disease, dementia, hereditary cerebellar ataxias, paraplegias, syringomyelia, phakomatoses, and much more. In fact, Layzer, Cecil Textbook of Medicine (article enclosed), states that "some degenerative diseases are difficult to classify because they involve multiple anatomic locations" (see page 2050). For example, Alzheimer's disease has traditionally been very difficult or impossible to prevent or even to treat effectively with chemotherapeutic agents. See e.g., the Cecil Textbook of Medicine, 20th edition (1996), Vol. 2, wherein it is stated that "[t]here is no cure for Alzheimer's disease, and no drug tried so far can alter the progress of the disease." (pg. 1994).

Thus, factors such as "sufficient working examples", "the level of skill in the art" and "predictability", etc. have been demonstrated to be sufficiently lacking in the use of the invention. In view of the breadth of the claim, the chemical nature of the invention, the unpredictability of ligand-receptor interactions in general, and the lack of working examples regarding the activity of the claimed compounds, one having ordinary skill in the art would have to undergo an undue amount of experimentation to use the invention commensurate in scope with the claims.

Applicant's remarks and declaration by Dr. Tani filed on January 8, 2004 are fully considered, but they are not deemed to be sufficient to provide enablement for the entire **scope** of the claims. It is emphasized that the specification does not enable any person skilled in the art to which it pertains, or with which it most nearly connected, to use the invention commensurate in scope with these claims where the disorder is treatable with a nicotinic acetylcholine receptor ligand. As provided in the previous office action, the instant claims encompass many disorders treatment of which is extremely difficult. Recent studies on experimental and clinical pharmacology of nicotinic acetylcholine receptors cited in Annual Reports in Medicinal Chemistry indicate that the following disorders may be associated with nicotinic acetylcholine receptors: senile dementia of the Alzheimer's type, Parkinson's disease, Huntington's chorea, tardive dyskinesia, hyperkinesias, mania, depression, attention deficit disorder, anxiety, dyslexia, schizophrenia, Tourette's syndrome and smoking cessation. The "nicotinic" effect with respect to Alzheimer's is hypothesized. Parkinson's Disease is "presently of unknown etiology" and recent studies have exhibited dosing problems as well as "unusually high placebo effects". The pathophysiology of Tourette's syndrome is unknown. Additionally, there are other pathological non-CNS conditions, such as pouchitis and influenza virus-induced pneuomonitis, where nicotinic efficacy has been reported, but remains to be confirmed.

It is difficult to treat many of the disorders claimed herein. Where the utility is unusual or difficult to treat or speculative, the examiner has authority to require evidence that tests relied on are reasonably predictive of *in vivo* efficacy by those skilled in the art. See for example *In re Ruskin* 148 USPQ 221; *Ex parte Jovanovics* 211 USPQ 907. Applicant has not provided any reference(s) that forms sufficient evidence that claimed uses were art-recognized based on

activity relied on at the time of applicants' effective filing date. MPEP 2164.05(a). When the best efforts have failed to achieve a goal, it is reasonable for the PTO to require evidence that such a goal has been accomplished, *In re Ferens*, 163 USPQ 609. Patent protection is granted in return for an enabling disclosure of an invention, not for vague intimations of general ideas that may or may not be workable. Tossing out the mere germ of an idea does not constitute enabling disclosure. The failure of skilled scientists to achieve a goal is substantial evidence that achieving such a goal is beyond the skill of practitioners in that art, *Genentech vs. Novo Nordisk*, 42 USPQ2nd 1001, 1006.

Allowable Subject Matter

Claims 35-36, 3-4, 22-25 and 34 are allowed. The instantly claimed compounds are not taught or suggested in the references of record, see e.g., U.S. Patent No. 4,588,722.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Deepak Rao whose telephone number is (571) 272-0672. The examiner can normally be reached on Tuesday-Friday from 6:30am to 5:00pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James O. Wilson, Acting-SPE of 1624, can be reached at (571) 272-0661. The fax phone number for the organization where this application or proceeding is assigned is (571) 273-8300.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (571) 272-1600.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Deepak Rao
Primary Examiner
Art Unit 1624

September 19, 2005